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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,678	11/28/2000	Kan-Hung Lee	TAI-3L6	7845

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EXAMINER

SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/724,678	Applicant(s) LEE ET AL.	
	Examiner Jehanne Souaya Sitton	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6-20, 27 and 28 is/are pending in the application.
- 4a) Of the above claim(s) 6-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27 and 28 is/are rejected.
- 7) ☒ Claim(s) 27, 28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 27 and 28 are pending in the instant application. Claims 6-20 stand withdrawn from consideration as being drawn to a non-elected intention. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient, in the absence of, for example, a declaration under 37 CFR 1.132 with regard to the unexpected results set forth in the arguments, to place this application in condition for allowance. The following rejections, while reiterated from the previous office action, are newly applied to the newly filed claims. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow.

Claim Objections

2. Claims 27 and 28 are objected to because of the following informalities: the claims recite Markush groups, however it is unclear in lines 26-28 of claim 27 and lines 10-12 of claim 28, if all of the probes are listed in the alternative or if SEQ ID NOS 9-14 are listed in the alternative but that the kit must contain SEQ ID NOS 15 and a degenerate sequence of any of SEQ ID NOS 12-15. The following recitation would be more clear, if the intention is to list all of the sequences for probes SEQ ID NOS 9-15 and degenerates of SEQ ID NOS 12-15:

In claim 27, lines 25 and 26, and in claim 28, lines 10 and 11, delete the word "and" and replace with the word --or--.

3. Additionally, claim 27 contains a typographical error as it appears that a hyphen (-) is missing between the numbers 12 and 15 of line 28.

Claim Rejections - 35 USC § 103

4. Claims 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kilpatrick (US Patent 6,168,917: 102(e) date July 9, 1999) in view of Accession numbers U22521 (Jan 1997), AF177911 (Sep 1999), AF136379 (Jun 2000), U55870 (May 1996) and Z78129 (Aug 1997) and further in view of Accession number E30248 (from JP 1999346799, published Dec 1999).

Kilpatrick teaches a method that uses specific primer pairs to detect different enterovirus serotypes, including enterovirus 71 and coxsackievirus A16 (see col.2, fig 5, col 11, table 1, and cols 16 and 17). Kilpatrick specifically teaches that there is a need for a detection system that identifies and differentiates most or all enterovirus serotypes and that such would improve the speed and accuracy of processing samples and increase the sensitivity of detecting minority populations of enteroviruses in mixed serotype cultures (col. 6, lines 31-35). Kilpatrick specifically teaches methods of developing suitable primer pairs, including the use of degenerate primer pairs which incorporate mixed base residues or deoxyinosine to increase the speed and sensitivity of detecting non polio enteroviruses (col. 7, lines 40-41, and col 15). Kilpatrick teaches an amino acid alignment of different non polio enteroviruses including enterovirus 71 and coxsackievirus A16 (fig 2a-2d) and further teaches that nucleotide sequences of such were known at the time of the invention (col. 10, lines 16-30). Kilpatrick teaches how to develop specific primer pairs to identify such serotypes in PCR based methods of detection and differentiation (col 11-13) using regions of differing nucleic acid sequence homology among nucleotide capsid sequences (col 12, lines 26-67 and col 10 lines 31-32) of different serotypes.

Art Unit: 1634

Further, Kilpatrick teaches providing primer pairs as well as probes fixed to a solid support in kit format for use in practicing the method of Kilpatrick (para bridging cols 13 and 14). It is noted that Kilpatrick does not teach primer pairs or kits comprising the claimed primer or probe sequences. However, the sequence of enterovirus 71 and coxsackievirus A16 were known in the art at the time of the invention, and specifically the following Accession numbers were available to the ordinary artisan: U22521 teaches the complete sequence of Enterovirus 71 BrCr, AF177911 teaches the coxsackievirus A16 polyprotein gene (which contains SEQ ID NO 14: positions 1346-1475, and SEQ ID NO 15, positions 1392-1422), AF136379 teaches Enterovirus 71 polyprotein mRNA, U55870 teaches an Enterovirus 5' non translated region sequence which contains SEQ ID NOS 10 and 11 and Z78129 teaches a region of Enterovirus 70 RNA 5' untranslated region (which contains SEQ ID NO 9). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to develop primer pairs and nucleotide sequences to detect Enterovirus 71 and Coxsackievirus A16 and to package such sequences in kit format as Kilpatrick specifically teaches primer pairs that detect specific serotypes including Enterovirus 71 and Coxsackievirus A16 and teaches packaging such in kit format. The ordinary artisan would have been motivated to develop such sequences as Kilpatrick specifically teaches a need for such a system. Although Kilpatrick in view of the recited accession numbers do not teach the specific primer pair and nucleotide sequences of the claimed invention, armed with the teachings of Kilpatrick, the ordinary artisan would have been able to develop primer pairs and nucleotide sequences that would specifically detect Enterovirus 71 and Coxsackievirus A16 given that the sequences of such serotypes were known in the art at the time of the invention and Kilpatrick specifically teaches how to develop specific primer pairs

Art Unit: 1634

and nucleotide sequences specific for certain serotypes (it is noted that accession number E30248 teaches the reverse complement of SEQ ID NO 7, which is used to identify serotypes of enterovirus). Such primer pairs and nucleotide sequences would be considered functionally equivalent in a method of detecting Enterovirus 71 and Coxsackievirus A16, absent evidence to the contrary.

Response to Arguments

5. The response traverses the rejection. The response asserts that the mere fact that references can be combined does not make combination obvious and that “obvious to try” is not the standard for establishing prima facie obviousness. Alone, these arguments would not be persuasive for the reasons already made of record in the examiner’s final rejection and advisory action. The response further asserts that the claims have been amended to provide kits containing oligonucleotide sequences “consisting” of the specific sequences set forth in the claims as well as SEQ ID NOS: 9-15 bound on a solid support. The response further submits unexpected and advantageous properties of the kits presented in claims 27 and 28. These arguments have been thoroughly reviewed but were not found persuasive as the arguments of counsel cannot take the place of evidence in the record. MPEP 716.01(c) states:

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

However, arguments with regard to the unexpected and improved sensitivity of the kits claimed in claims 27 and 28 would be persuasive if filed in an appropriate affidavit or declaration. Such evidence, in view of the amendment to the claims to provide kits comprising primer pairs and

Art Unit: 1634

support bound probe nucleic acid sequences “consisting of” the sequences recited in the claims and also because Kilpatrick does not specifically demonstrate primer pairs and probes to Vp2, would overcome the rejection. [The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations made are correct as provided by 35 U.S.C. 25 and 18, U.S.C. 1001. In *Ex parte Gray* (10 USPQ2d 1923) the Courts held that conclusory statements made in publications could not substitute for a declaratory evidence filed under 37 CFR 1.132. Furthermore, in *Ex parte Ishizaka* (BdPatApp&Int 24 USPQ2d 1621), the Courts stated that 37 CFR 1.132 does not recognize the use of a publication as a substitute for a declaration. Consequently, a Declaration filed under 37 CFR 1.132 sworn by at least one of the instant inventors which cites/explains the relevant parts of the Shih et al reference would overcome the rejection.]

Conclusion

6. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. In the event of rejoinder, the requirement for restriction between the product claims and

Art Unit: 1634

the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined.

See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

As none of the withdrawn method claims presently contain all of the limitations of claims 27 and 28, were claims 27 and 28 to be found allowable (if the conditions set forth in section 5 above were met), the examiner suggests the following method claims:

A method for detecting and differentiating an enterovirus in a sample comprising:

- a) contacting nucleic acids in the sample with a pair of primers wherein a first primer of said pair consists of a sequence of any of SEQ ID NOS: 1-5, or a degenerate sequence of SEQ ID No: 5 and a second primer of said pair consists of a sequence of any of SEQ ID NOS: 6-8, or a degenerate sequence of SEQ ID No: 8, provided that the second primer consists of the sequence of SEQ ID NO: 8 or a degenerate sequence thereof when the first primer consists of the sequence of SEQ ID NO: 5 or a degenerate sequence thereof; and
- b) contacting the amplification product generated in step a) with at least one synthetic nucleotide sequence fixed on a solid substrate wherein the synthetic nucleotide sequence comprises any sequence selected from the group consisting of SEQ ID NOS: 9-15, or a degenerate sequence of any of SEQ ID NOS 12-15 and detecting hybridization, thereby detecting and differentiating an enterovirus in the sample.

A method for detecting and differentiating an enterovirus in a sample comprising contacting nucleic acids in a sample with at least one synthetic nucleotide sequence fixed on a solid substrate wherein the synthetic nucleotide sequence comprises any sequence selected from the group consisting of SEQ ID NOS: 9-15, or a degenerate sequence of any of SEQ ID NOS 12-15 and detecting hybridization, thereby detecting and differentiating an enterovirus in the sample.

7. No claims are presently allowable over the closest prior art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-

Art Unit: 1634

0572. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (571) 272-0507.



Jehanne (Souaya) Sitton
Primary Examiner
Art Unit 1634

2/6/04